ACID–BASE CHARACTERISTICS OF 2-ACYL-3(5)-HYDROXYISOXAZOLIDINES IN A HYDROGEN BOND

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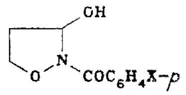
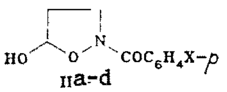
In solution hydroxyisoxazolidines form intermolecular hydrogen bonds. For 3-hydroxyisoxazolidines the proton acceptor is the oxygen atom of the hydroxyl group, and for the 5-hydroxy compounds it is the cyclic oxygen atom. These compounds are close to phenol with respect to the relative acidity in the hydrogen bond.

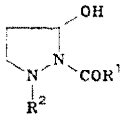
In [1] we demonstrated the possibility of studying the acid–base characteristics of hydroxyazolidines in a hydrogen bond as illustrated by 1-acyl-5-hydroxypyrazolidines. In the present work we used IR spectroscopy to determine the acid–base characteristics of the isomeric 3- and 5-hydroxy-2-acylisoxazolidines (I) and (II) containing semiaminal and semiacetal fragments, respectively (their synthesis was described in [2]).



Ia-c. e



IIa-d



III

I, IIa $X=H$; b $X=Br$; c $X=CH_3$; d $X=OCH_3$; e $X=NO_2$

The spectral behavior of compounds (I) and the previously investigated derivatives (III) and of their aroyl derivatives, in particular, is largely similar (Fig. 1). The hydrogen bond has only intermolecular character (the dependence of the absorption band of the OH group on the concentration), and the carbonyl group is not the donor center of the hydrogen bond. (Its absorption does not change when c = 0.150-0.005 M.) The shift of the hydroxyl band in the self-associates amounts to 180-200 cm^{-1} both for compounds (I) and (III) (Table 1). The high-frequency absorption band of the hydroxyl group in compounds (I) is significantly broadened ($\Delta\nu_{1/2} = 70$ cm^{-1}) and is shifted toward the low-frequency region (~3560 cm^{-1}) compared with the absorption band of the free hydroxyl group, which is observed at 3580 cm^{-1}, for example, in the 1-acetyl derivatives (III) ($\Delta\nu_{1/2} = 42$ cm^{-1}). The symmetrical form of the high-frequency curve and subsequent graphical separation (Fig. 1) made it possible to isolate the two absorption bands of the hydroxyl group, i.e., a free group (at 3580 cm^{-1}) and a group combined by an intramolecular hydrogen bond, presumably, with the π system of the aromatic ring [3] (at 3540 cm^{-1}). The above-mentioned relationships governing the spectral behavior of (I) and (III) make it possible to suppose that the hydrogen bonds in the self-associates are similar in nature; the proton acceptor is evidently also the oxygen atom of the hydroxyl group in compounds (I).

The relative acidity of (I), measured by the method of Iogansen [4] by analogy with the pyrazolidine (III) [1] in an inert solvent with THF as organic base, and the relative acidity of (III) are similar in value. Thus, the average value of the acidity for the derivatives of (I) is $p_i \sim 0.85$ (Table 2), and for pyrazolidine (III), $p_i \sim 0.82$ (for phenol $p_i = 1$).

The "basicity" of compounds (I) was investigated for the case of 2-benzoyl-3-methoxyisoxazolidine, which does not have a true proton-donating center and is a base close to unity in strength. Phenol was used as standard acid. On the basis of the obtained data ($-\Delta\nu_{OH} = 232$ cm^{-1}, $-\Delta H$ 4.57 kcal/mole) we obtained the "basicity" $\varepsilon_j = 0.87$ [for (III), $\varepsilon_j = 0.96$, with reference to diethyl ether $\varepsilon_1 = 1$]. It should be noted that, as in the (I) and (III) series, the carbonyl group of this compound does not take part in the formation of a complex with phenol, since, according to published data [5, p. 111], $\Delta\nu_{OH} = $ ~300 cm^{-1} for the

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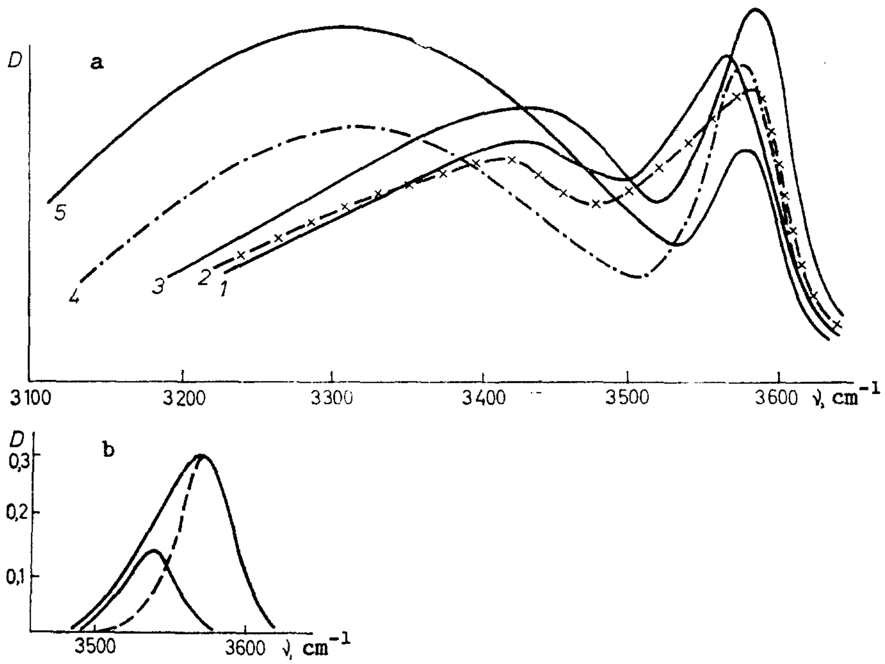


Fig. 1. IR spectra of 2-acyl-3(5)-hydroxyisoxazolidines in the ν_{OH} region. a. 1) Compound (III); 2) compound (Ia); 3) compound (Ib); 4) compound (IIb); 5) compound (IIc). b. Graphical separation of the high-frequency ν_{OH} of compound (Ia).

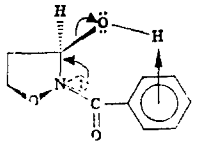
TABLE 1. Spectral and Thermodynamic Characteristics of the Self-Associates of (I) and (II)

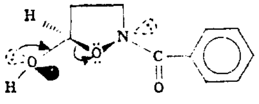
Compound	ν_{OH}, cm^{-1}	$\Delta\nu_{OH}$, cm^{-1}	$-\Delta H$, kcal/mole	ν_{CO}, cm^{-1}
I^a	3380	200	4,17	1650
Ib	3400	180	3,90	1640
Ie	3390	190	4,04	1660
IIa	3322	258	4,88	1650
IIb	3317	263	4,92	1645
IIc	3296	285	5,15	1650
II^d	3310	270	5,00	1645

TABLE 2. Characteristics of the Complexes of 2-Acyl-3(5)-hydroxyisoxazolidines (I) and (II) with THF

Complex	ν_{OH}, cm^{-1}	$\Delta\nu_{OH}$, cm^{-1}	$-\Delta H$, kcal/mole	p_i
Ia + THF	3330	250	4,78	0,87
Ib + THF	3350	230	4.54	0,82
IIa + THF	3308	270	5,00	0,91
IIb + THF	3308	268	5,00	0,91
IIc + THF	3316	264	4,90	0,90
IId + THF	3300	280	5,10	0,92

complex of phenol with benzamides. The proton acceptor here is also the oxygen atom of the alkoxy group (3-OR). Such general behavior of the compounds in the two series (I, III), containing a semiaminal fragment, is evidently due largely to the similar stereoelectronic effects in these two types of molecules [6, p. 169; 7].





The nature of the hydrogen bond in the 2-acyl-5-hydroxyisoxazolidines (II), which are cyclic semiacetals, differs appreciably from that in the compounds with the aminal fragment (I, III). This shows up primarily in an increase of the shift of the absorption band for the hydroxyl group during the formation of the hydrogen bond in the self-associates to 250 cm^{-1} and is a test for the assignment of the isomers to series (I) or series (II) (Fig. 1). A hydrogen bond with the π system of the aromatic ring is not formed here. Therefore, as also for the 1-acetylpyrazolidines (III), the absorption band of the free hydroxyl group lies at 3580 cm^{-1}. (It has Lorentz form $\Delta\nu_{1/2}$ = 42-44 cm^{-1}.) The carbonyl group is also not the donor center of the intermolecular hydrogen bond in this series of compounds. (The concentration dependence is absent for $\nu_{C=O}$, but is present for

ν_{OH}.) The increase in the shift of the absorption band of the hydroxyl group in the self-associates may indicate an increase in the relative "acidity" or "basicity" of the molecule. Our measurements showed that the "acidity" is in fact increased somewhat ($p_i \sim 0.91$), but the "basicity" is increased substantially more (ε_j 0.94).* This made it possible to suppose that the proton acceptor in the hydrogen bond of compounds (II) is evidently the cyclic oxygen atom and not the oxygen atom of the hydroxyl group as for the derivatives of (I) and (III). In fact, the shifts of hydroxyl band are extremely close in the self-associates and in the complexes of the derivatives of (II) with THF. The same donor center is observed in the complex of the methoxy derivative (II) with phenol. The main reason for the increase in the electron density at the cyclic oxygen atom in compounds (II) compared with (I) is evidently the presence of an exo-anomeric effect in addition to the gauche-effect common to (I) and (II) [6].

EXPERIMENTAL

The IR spectra were measured on a Specord IR-75 instrument (GDR). The scan rate was 100 cm^{-1}/2.6 min; the recording scale was 10 mm/10 cm^{-1} in the region of 1600-1700 cm^{-1} and 5 mm/10 cm^{-1} in the region of 3200-3650 cm^{-1}. In methylene chloride c = 0.1500-0.0015 M. Calcium chloride cuvettes with constant thickness between 0.1 mm and 20 mm were used. To determine the $\Delta\nu$ values in the self-associates and the "basicity" and "acidity," we obtained the center of gravity of the absorption bands. The acid–base characteristics of the unassociated compounds (I) and (II) were measured for dilute solutions (0.02-0.03 M) in an inert solvent with a THF concentraton of 1 M. The acidity factor was calculated by means of the equation [4]: $p_i = (\Delta H_{ij})/(\Delta H_{11}\varepsilon_j)$, where ΔH_{ij} is the enthalpy of the hydrogen bond; $-\Delta H = 0.33\sqrt{\Delta\nu - 40}$ [8]; $\Delta H_{11} = 5.3$ (the enthalpy of the standard complex of phenol with diethyl ether); ε_j is the basicity factor (for THF, $\varepsilon_j = 1.04$). The average $\Delta\nu_{OH}$ values are given with an accuracy of ±10 cm^{-1}, and this leads to an error of ±0.015 in the determination of p_i.

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*The basicity was measured for 2-benzoyl-5-methoxyisoxazolidine ($\Delta\nu_{OH} = 268$ cm^{-1}, $-\Delta H = 4.99$ kcal/mole) with phenol.